

**AMENDMENTS TO THE CLAIMS**

1. **(Currently Amended)** A substantially pure polypeptide ~~fragment~~ which comprises an amino acid sequence encoded by a member of the *esat-6* gene family or comprises an amino acid analogue having a sequence identity with a polypeptide ~~fragment~~ encoded by a member of the *esat-6* gene family of at least ~~94~~70% and at the same time being immunologically equivalent to the polypeptide ~~fragment~~ encoded by a member of the *esat-6* gene family, with the proviso that the substantially pure polypeptide is not selected from the group consisting of Rv0287, Rv0288, Rv1037c, Rv1038c, Rv1197, Rv1198, Rv1792, Rv1793, Rv2346c, Rv2347c, Rv3019c, Rv3619c, Rv3620c, Rv3874, and Rv3875.

2. **(Currently Amended)** A substantially pure polypeptide ~~fragment~~ which comprises ~~an~~ the amino acid sequence ~~as shown set forth~~ in SEQ ID NOS: 7, 13, 15, 17, 19, 21, 23, 25, 27, 29 or 31 or comprises an amino acid sequence analogue having a sequence identity with a polypeptide ~~fragment~~ selected from the group consisting of SEQ ID NOS: 7, 13, 15, 17, 19, 21, 23, 25, 27, 29 and 31 of at least 70% and at the same time being immunologically equivalent to the polypeptide ~~fragment~~ selected from the group consisting of SEQ ID NOS: 7, 13, 15, 17, 19, 21, 23, 25, 27, 29 and 31.

3. **(Currently Amended)** A substantially pure polypeptide ~~fragment~~ which comprises a T-cell epitope of the amino acid sequence ~~as shown set forth~~ in SEQ ID NOS: 7, 13, 15, 17, 19, 21, 23, 25, 27, 29 or 31 or has a sequence identity of at least 70% with a T-cell epitope of the amino acid sequence and at the same time being immunologically equivalent to said polypeptide ~~fragment~~.

4. **(Currently Amended)** The polypeptide ~~fragment~~ according to any of the preceding claims in essentially pure form.

5. **(Currently Amended)** The polypeptide ~~fragment~~ according to claim 1, which has a length of at least 7 amino acid residues, such as at least 8, at least 9, at least 10, at least 12, at least 14, at least 16, at least 18, at least 20, at least 22, at least 24, and at least 30 amino acid residues.

6. **(Currently Amended)** The polypeptide ~~fragment~~ according to claim 1 which is free from any signal sequence.

7. **(Currently Amended)** A polypeptide ~~fragment~~ according to claim 1, wherein the said sequence identity is at least 80%, such as at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%,   , at least 96%, at least 97%, at least 98%, at least 99%, and at least 99.5%.

8. **(Currently Amended)** A fusion polypeptide comprising at least one polypeptide ~~fragment~~ according to claim 1 and at least one fusion partner.

9. **(Currently Amended)** A fusion polypeptide according to claim 8, wherein the fusion partner is selected from the group consisting of a polypeptide ~~fragment~~ as defined in any one of claims 1-3 and 5-7, and another polypeptide ~~fragment~~ derived from a bacterium belonging to the tuberculosis complex, such as ESAT-6 or at least one T-cell epitope thereof, TB10.4 or at least one T-cell epitope thereof, and MPT59 or at least one T-cell epitope thereof.

10. **(Currently Amended)** A fusion polypeptide ~~fragment~~ according to claim 8, wherein the fusion partner is selected from the group consisting of DnaK, GroEL, urease, glutamine synthetase, ~~the proline-rich complex~~, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, HBHA (heparin binding hemagglutinin), MPT51, superoxide dismutase, ~~19 kDa lipoprotein~~,  $\alpha$ -crystallin, GroES, and MPT59.

11. **(Original)** A polypeptide according to claim 1 which is lipidated so as to allow a self-adjuvating effect of the polypeptide.

12. **(Original)** A substantially pure polypeptide according to claim 1 for use as a pharmaceutical.

13. **(Canceled)**

14. **(Currently Amended)** An immunologic composition comprising at least one polypeptide according to claim 1.

15. **(Original)** An immunologic composition according to claim 14, which further comprises an immunologically and pharmaceutically acceptable carrier, vehicle or adjuvant.

16. **(Original)** An immunologic composition according to claim 15, wherein the carrier is selected from the group consisting of a polymer to which the polypeptide(s) is/are bound by hydrophobic non-covalent interaction, such as a plastic, e.g. polystyrene, a polymer to which the polypeptide(s) is/are covalently bound, such as a polysaccharide, and a polypeptide, e.g. bovine serum albumin, ovalbumin or keyhole limpet hemocyanin; the vehicle is selected from the group consisting of a diluent and a suspending agent; and the adjuvant is selected from the group consisting of dimethyldioctadecylammonium bromide (DDA), Quil A, poly I:C, Freund's incomplete adjuvant, IFN- $\gamma$ , IL-2, IL-12, monophosphoryl lipid A (MPL), and muramyl dipeptide (MDP).

17. **(Currently Amended)** An immunologic composition according to claims 14-16, comprising at least two different of said polypeptides fragments, ~~each different polypeptide fragment being a polypeptide according to claim 1.~~

18. **(Currently Amended)** An immunologic composition according to claim 17, comprising 3-20 different of said polypeptides fragments.

19. **(Canceled)**.

20. **(Canceled)**

21. **(Canceled)**

22. **(Canceled)**

23. **(Canceled)**

24. **(Canceled)**

25. **(Canceled)**

26. **(Canceled)**

27. **(Currently Amended)** A composition for diagnosing tuberculosis in an animal, including a human being, comprising a polypeptide according to claim 1, ~~optionally in combination with a means for detection.~~

28. **(Withdrawn)** A nucleic acid fragment in isolated form which

- 1) comprises a nucleic acid sequence which is a member of the *esat-6* gene family,
- 2) has a length of at least 10 nucleotides and hybridizes under moderately stringent conditions with a nucleic acid fragment which has a nucleotide as disclosed in SEQ ID NOs: 6, 12, 14, 16, 18, 20, 22, 24, 26, 28 or 30 or a sequence complementary thereto,

29. **(Withdrawn)** A nucleic acid fragment according to claim 28, which is a DNA fragment.

30. **(Withdrawn)** A nucleic acid fragment according to claim 28 or 29 for use as a pharmaceutical.

31. **(Withdrawn)** The use of a nucleic acid fragment according to claim 28 or 29 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against tuberculosis caused by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*.

32. **(Withdrawn)** A vaccine comprising a nucleic acid fragment according to claim 28 or 29, the vaccine effecting *in vivo* expression of antigen by an animal, including a human being, to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the tuberculosis complex in an animal, including a human being.

33. **(Withdrawn)** A replicable expression vector which comprises a nucleic acid fragment according to claim 28 or 29.

34. **(Withdrawn)** A vector according to claim 33, which is selected from the group consisting of a virus, a bacteriophage, a plasmid, a cosmid, and a microchromosome.

35. **(Withdrawn)** A transformed cell harbouring at least one vector according to claim 33.

36. **(Withdrawn)** A transformed cell according to claim 35, which is a bacterium belonging to the tuberculosis complex, such as a *M. tuberculosis bovis* BCG cell.

37. **(Withdrawn)** A transformed cell according to claim 35, which expresses a polypeptide according to claim 1.

38. **(Withdrawn)** A composition for diagnosing tuberculosis in an animal, including a human being, comprising a nucleic acid fragment according to claim 23 or 24, optionally in combination with a means for detection.

39. **(Withdrawn)** A method for producing a polypeptide according to claim 1, comprising inserting a nucleic acid fragment according to claim 28 into a vector which is able to replicate in a host cell, introducing the resulting recombinant vector into the host cell, culturing the host cell in a culture medium under conditions sufficient to effect expression of the polypeptide, and recovering the polypeptide from the host cell or culture medium; or

isolating the polypeptide from whole mycobacteria of the tuberculosis complex or from lysates or fractions thereof, e.g. cell wall containing fractions; or

synthesizing the polypeptide by solid or liquid phase peptide synthesis.

40. **(Withdrawn)** A method for producing an immunologic composition comprising

preparing, synthesizing or isolating a polypeptide according to claim 1, and  
solubilizing or dispersing the polypeptide in a medium for a vaccine, and  
optionally adding other *M. tuberculosis* antigens and/or a carrier, vehicle and/or adjuvant  
substance,

or

cultivating a cell according to claim 35, and  
transferring the cells to a medium for a vaccine, and  
optionally adding a carrier, vehicle and/or adjuvant substance.

41. **(Withdrawn)** A method for immunising an animal, including a human being, against tuberculosis caused by mycobacteria belonging to the tuberculosis complex, comprising administering to the animal the polypeptide according to claim 1, the immunologic composition according to claim 19, or the vaccine according to claim 26.

42. **(Withdrawn)** A method according to claim 41, wherein the polypeptide, immunologic composition, or vaccine is administered by the parenteral (such as intravenous and intraarterially), intraperitoneal, intramuscular, subcutaneous, intradermal, oral, buccal, sublingual, nasal, rectal or transdermal route.

43. **(Withdrawn)** A method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the tuberculosis complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the animal with the polypeptide according to claim 1, a significant release into the extracellular phase of at least one cytokine by mononuclear cells in the blood sample being indicative of the animal being sensitized.

44. **(Withdrawn)** A monoclonal or polyclonal antibody, which is specifically reacting with a polypeptide according to claim 1 in an immuno assay, or a specific binding fragment of said antibody.

45. **(Withdrawn)** A method of diagnosing tuberculosis caused by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis* in an animal, including a human being,

comprising intradermally injecting, in the animal, a polypeptide according to claim 1 or an immunologic composition according to claim 20, a positive skin response at the location of injection being indicative of the animal having tuberculosis, and a negative skin response at the location of injection being indicative of the animal not having tuberculosis.

46. **(New)** A polypeptide according to claim 1, wherein said sequence identity is at least 96%.

47. **(New)** A polypeptide according to claim 1, wherein said sequence identity is at least 97%.

48. **(New)** A polypeptide according to claim 1, wherein said sequence identity is at least 98%.

49. **(New)** A polypeptide according to claim 1, wherein said sequence identity is at least 99%.

50. **(New)** A polypeptide according to claim 1, wherein said sequence identity is 100%.

51. **(New)** The diagnostic composition of claim 27, further comprising a nucleic acid probe capable of detecting a nucleic acid molecule that encodes the *esat-6* polypeptide of claim 1.